

Wyeth (John) & Bro.

THE TWO NEW CHOLAGOGUES
EUONYMUS ATROPURPUREUS (WAHOO),
AND
IRIS VERSICOLOR (BLUE FLAG).

An important and interesting paper, by Dr. J. R. Black, of Newark, Ohio, published in the *Philadelphia Medical and Surgical Reporter* for April 19, 1879, attracted attention to the valuable medicinal properties of the Fluid Extract of *Euonymus Atropurpureus*, or Wahoo, and especially to our preparation of it, which was the one employed by him. A largely increased demand upon us for this article was the result; and we were led to institute, through some of our ablest practitioners, experiments and investigations which have fully confirmed the assertions of Dr. Black. We ascribe the superiority of the preparation supplied by us to the fact that we use in its manufacture the bark of the root only, employing a menstruum that we have found by experience, thoroughly extracts all the medicinal properties of the drug. The results attained with an article so prepared, are, according to all the testimony available, superior to those from the resinoid alone. Thus the favorable opinions expressed by Bartholow, Rutherford, and other writers, based upon the experience they had had with the resinoid, are of much greater force in support of our claims for our Elixir and Fluid Extract, which contain all the active principles of the plant.

Our attention has also been drawn to the preparation, for medicinal use, of another vegetable product, of an analogous kind, viz.: the *Iris Versicolor*, or Blue Flag. Long known to the Indians, as a remedy, this plant has been extensively employed by eclectic practitioners, and only within a few years have the regular profession begun to recognize its virtues. These virtues are, according to the evidence of competent observers, superior to those of *Podophyllin*, which has acquired such favor as a cholagogue. We prepare this article in the same way, in the form of Elixir and Fluid Extract, and claim the same superiority for it over the resinoid, as in the case of Wahoo.

In regard to both these articles, we would say that we follow our inexorable rule of having the selection of the crude material made with the utmost care, and observing the most scrupulous exactness in every stage of the manipulation, so as to produce an agent that shall not disappoint the prescriber.

Our claims, supported by authority such as that of Bartholow, Rutherford, Black, and others, will, we are confident, be borne out by the test of practice, which we ask physicians to institute; and we beg their careful perusal of the following statements in regard to the above named drugs.

Yours, very respectfully,

JOHN WYETH & BRO.



EUONYMUS ATROPURPUREUS.

WAHOO.

The bark is the portion of the plant employed in the preparation of medicinal agents. The bark of the root, only, should be used in pharmaceutical processes, for this is richer in the active constituents than the bark of any other part of the shrub.

History: *Euonymus Europæus* has long been cultivated in gardens because of the brilliant red color of the fruit, which has given to the shrub one of its common names—*burning bush*. *Euonymus Americanus* has, also, been cultivated as an ornamental shrub. The latter has been used in preparing medicinal agents instead of *E. Atropurpureus*, but although they possess analogous properties, such substitution must be regarded as a sophistication. According to the U. S. Dispensatory, *E. Europæus* has been examined by Grundner, who found it to possess diuretic properties only; but an oil obtained from the seeds was used to destroy vermin and as a stimulating application to old ulcers. According to Griffith, “the seeds of these varieties are emetic and purgative, and the leaves are poisonous to sheep and other animals.”

Through the West and South, under the name of *Wahoo*, *E. Atropurpureus* has long been used in domestic practice. This name, as well as the knowledge of its uses was, doubtless, obtained from the Indians by the primitive settlers, in search of remedies for the diseases incident to a new country. It was used by them as a purgative, diuretic, and alterative, especially the last, because it was supposed to possess great powers as a “blood purifier.” We owe its introduction into medical practice to the Eclectic physicians, who have been diligent students of our indigenous *Materia Medica*. They adopted the aboriginal and domestic notions in regard to its use, and have for several years employed it as a purgative, diuretic, and alterative. Beside the Dispensatories, the works of the regular medical profession have only lately taken any notice of this, now, promising remedy. It is contained in the “Secondary List,” of the U. S. Pharmacopœia. In Bartholow’s *Treatise on Materia Medica and Therapeutics* it is referred to and its powers defined briefly. It has been the subject of investigation by several pharmacutists, Wenzell and Clothier; its physiological actions have been studied by Rutherford, and its medical properties have been set forth in a special memoir by Dr. J. R. Black.

Composition and Properties: The first systematic study of its composition was made by Mr. William P. Clothier, who in 1861, published an inaugural essay in *The American Journal of Pharmacy*, p. 490. He ascertained that it contained starch, sugar, gum, pectin, indifferent substances, an oleo-resin, and a bitter principle crystallizing in "yellow, acicular crystals." A year subsequent to these researches, Mr. W. T. Wenzell undertook the examination of the bark anew, and as his processes were better, it is probable that his results are more to be depended on. Beside various unimportant ingredients, Wenzell separated a bitter, non-crystallizable principle, neutral in reaction, which he named, *Euonymin*; he also discovered a principle identical with *Asparagin*, an *oleo-resin* of complex constitution, an acid peculiar to *Euonymus*, which he termed *Euonic acid*, and various other constituents. (*American Journal of Pharmacy*, 1862, p. 390, Vol. 34.)

These analyses are very important, as they demonstrate the numerous and valuable constituents found in *Euonymus*, and afford abundant support to the theory of its utility in disease. A drug possessed of such constituents must have important uses.

We learn from domestic practice and from the experience of those physicians who have tried it, that it acts as a purgative of a peculiar kind. Some liken it to Rhubarb, some to Castor oil, but as we shall see, it differs from both of these in important particulars. Most of the trials have been made with the preparation introduced by the Eclectic practitioners, and known as *Euonymine*, which is not an active principle, but consists of the oleo-resin mixed with variable proportions of *Euonymin* and *Asparagin*. The Eclectic "*Euonymine*" is obtained by precipitation of a concentrated tincture by water—the precipitate consisting of the parts named above, and when dried, is a brownish powder having an intensely bitter taste. When this *Euonymine* is taken in doses of about five grains, it causes free evacuations, characterised by certain peculiarities to be mentioned hereafter. It is obvious, however, that this preparation does not represent the full powers of the remedy. Much of the active principle, and other important ingredients, are lost in this process. A properly made fluid extract of the bark of the root is the true preparation, for in this are retained all of the constituents. A fluid extract of the bark of the root will contain not only the purgative principle, but the diuretic and so called alterant properties.

The valuable uses of *Euonymus* are set forth briefly by Barthorow, the first one to indicate the precise nature of its powers, as a remedy acting similarly to rhubarb and possessed of special activity as a hepatic stimulant. (*Practical Treatise on Materia Medica and Therapeutics*,

3d Ed., p. 484.) The most important contribution yet made to our knowledge of the physiological action of Euonymus, is the research of Rutherford and Vignal, undertaken for the British Medical Association. Amongst the cholagogues examined by them, Euonymine, the Eclectic preparation, stands in almost the first position as an agent stimulating the hepatic secretion. (*The British Medical Journal*, June, 1877). Mr. C. A. Santos, in some remarks on the chemical properties of Euonymus, states that it is a "diuretic, tonic, antiperiodic, and hydragogue cathartic," and that it has "beneficial effects in the different forms of dropsy." According to Mr. Clothier this remedy was introduced in Philadelphia by Mr. G. W. Carpenter as a remedy for dropsy, he having ascertained that it was largely used in the West for this purpose.

A recent and most important contribution to the therapeutical use of Euonymus is that of Dr. J. R. Black, of Newark, Ohio, (*The Medical and Surgical Reporter*, April 19, 1879,) who points out that "it acts as a gastric tonic, cholagogue and mild cathartic, and usually within two hours after its administration. Its action is unattended by nausea, griping, or any debilitating influence." Furthermore, he says, "the stools indicate the large presence of bile," which is a striking clinical confirmation of the laboratory experiments of Rutherford and Vignal. Again—"it is preëminently, the most unobjectionable of cathartics to overcome habitually loaded abdominal viscera * * especially is it of eminent service, when, from a variety of causes, hepatic and intestinal torpor are confirmed. * * Continued use does not habituate and blunt the system to its energy, consequently, the dose does not require to be increased. Black finds that "the fluid extracts of this drug in the market are of unequal strength," and that made from the bark of the root, is twice the strength of that prepared from the bark of the shrub. In this Dr. Black is undoubtedly correct, as all testify on this point who have made chemical investigations of both the bark of the root, and bark of the shrub.

"In summing up," says, Dr. Black, "it may be said that in Euonymus we have an invaluable gastric tonic, mild cholagogue. pleasant laxative or cathartic, according to the dose."

We have called on a practical therapeutist of much experience for an opinion as to the real value of this remedy, which we subjoin :

"Physiological experiment and clinical experience agree in the view that Euonymus is a stimulant to the liver,—a cholagogue—of special power. It is therefore a very satisfactory remedy in cases of torpor of the liver, in congestion of the liver, in jaundice from catarrh of the bile ducts, in ascites from obstructive disease of the liver. It is

much more effective than mercurials, and entirely free from their objectionable features.

"As a bitter, it acts as a tonic to the stomach, promotes appetite and digestion, and is peculiarly valuable because, as a hepatic stimulant, it promotes the intestinal digestion, the solution and absorption of fats, etc. Euonymus is, for these reasons, specially desirable in the gastro-intestinal and hepatic disorders succeeding to attacks of malarial fever. It possesses quite considerable antiperiodic power, and is therefore a valuable adjunct to quinia in the treatment of intermittent and remittent fevers. That it is a serviceable diuretic, there can be no doubt. It is useful in the dropsy of malaria, and in cardiac dropsy, but its most important application in this direction is as a remedy for ascites, and as a hdragogue."

Since the above was in print the following in regard to Euonymus has appeared in the *Lancet*, from Dr. W. M. Collins, of London:

Having recently made a trial of Euonymin in some cases of hepatic derangement, with defective secretion of bile, I am induced to offer a few brief remarks on its action as a cholagogue.

Euonymin, which has lately been brought into notice by the experiments of Dr. Rutherford, as a hepatic stimulant, is a resinous substance obtained from a species of Euonymus (Wahoo Bark). It differs from most of the ordinary so-called cholagogues, in not producing any intestinal irritation, its action on the liver being direct. It, therefore, does not give rise to the colicky pains and discomfort which so often attend the use of Podophyllin, and which tend to prove that the latter drug acts only indirectly on the liver by the irritation it sets up in the duodenum, for which portion of the intestine it has a special affinity. Euonymin is particularly serviceable in cases of hepatic dyspepsia, or what are commonly called attacks of "biliousness," with furred tongue, pale stools, lassitude, and general *malaise*, and under its use the tongue cleans, the stools become darker, and the feeling of languor and heaviness disappears. Its action is slow, and its effects experienced most about forty-eight hours after it has been taken. In too large or too frequent doses it may cause some depression. In most classifications of remedies met with in therapeutical works there is no special division made of cholagogues, but those remedies which are supposed to act on the liver are classified under other heads; *e. g.*, Podophyllin is included with the cathartics, and, perhaps, properly so, as this remedy only exercises a secondary action on the liver by catharsis. But Euonymin, and probably Iridin also, as shown by the recent experiments of Dr. Rutherford, may be considered as true cholagogues or hepatic stimulants, since they act directly on the liver.

IRIS VERSICOLOR.

BLUE FLAG.

History: Iris Versicolor, or Blue Flag, is indigenous to this country. Although belonging to the same family as Iris Florentina and other species of Iris growing in the south of Europe, it possesses very different powers. The portion of the plant employed in the preparation of pharmaceutical products, is the rhizoma, or root stalk, which is most active in the fresh state. This has long been known to possess cathartic and diuretic properties, but a careful investigation of its real properties has been made only recently. As was the case with its congener Euonymus, the knowledge of its uses was obtained by the pioneers from the Indians, who had learned by experience of its curative effects in certain conditions of disease. Since the first settlement of this continent Iris has been used more or less by regular physicians, cognizant of its powers, but its actual introduction into practice and its popularization as a remedy we owe to the Eclectics. These practitioners have always maintained that Iris had special power as a cholagogue, or bile stimulant, and have used it with success in disease of the liver, as a stomachic tonic, and as a diuretic. After all, this application of Iris is a mere confirmation of the notions entertained by the aborigines of its properties. It has been recognized by the U. S. Pharmacopœia, as a remedy, but is borne on the Secondary List as a substance of secondary importance. The U. S. Dispensatory gives the uncertain and desultory opinions of various practitioners in respect to its properties and uses. Bartholow is the only one amongst our systematic authors, who appears to have correct notions of the real utility of this agent. He remarks "There is much evidence tending to show that this remedy is really serviceable when the stools are clay-colored, and the skin jaundiced, in consequence of duodenal catarrh and obstruction of the biliary ducts. It is said that malarial jaundice may be cured by this drug, and that in bilious remittent fever and in chronic malarial poisoning it exerts a favorable influence." (*Practical Treatise on Materia Medica and Therapeutics*, p. 484). A writer on the editorial corps of the *London Lancet* had so long ago as 1862, *Lancet*, Aug. 30, 1862, correctly indicated the range of its pow-

ers. Speaking of Iridin, he says,—“Its action is that of a mild aperient cholagogue, and it is alleged to be diuretic, and indeed to excite all of the secretory organs. ‘Physicians,’ says one writer, ‘occasionally meet with patients upon whom podophyllin, even in small doses, exerts a powerful and long-continued influence, not easily obviated: in such cases Iridin seems to be more especially, indicated.’ In our hands Iridin has produced effects very similar to those occasioned by a combination of blue pill, rhubarb, and aloes. It seldom fails to produce mild catharsis with bilious evacuations; and appears to possess the advantages of (1) not requiring the addition of a mercurial, (2) not irritating the rectum as aloes is apt to do, and (3) it has no astringency, and therefore does not produce subsequent costiveness like rhubarb when given alone. In a sluggish state of the bowels arising from torpidity of the liver, or when the stools are pale, particularly as we find them in the intervals of overt attacks in gouty persons, we have found the Iridin one of the best aperients—much gentler than podophyllin, and more reliable when a slight cholagogue action is required to be maintained for a lengthened period.”

It is remarkable how this strong testimony to the peculiar powers and properties of Iris, derived from clinical experience and observation, is supported by physiological experiment. In that remarkable series of investigations into the action of cholagogues, undertaken by Rutherford, and which has thrown so much light on the actions of Euonymus, Iris was also examined into with the same care and accuracy, and with results that entirely confirm the deductions of clinical experience. We quote from the report (*The British Medical Journal*, June, 1877). “Iridin * * very powerfully stimulated the liver. * * It is also a decided stimulant of the intestinal glands. Judging from these experiments its irritant effects on the intestinal mucous membrane are decidedly less than those of podophyllin, while the purgative effects are greater than in the case of Euonymin. It is, also, more powerful in its effects on the liver than Euonymin. There seems every reason why this substance should be removed from its present obscurity and placed in a prominent position in practical medicine.”

In a recent article (*The Practitioner*,—London,—November, 1879,) on the “Physiological Actions of Drugs on the Secretion of Bile,” Rutherford sums up anew his conclusions on the actions and relative merits of Euonymin and Iridin.

“These two substances are prepared respectively from the roots of the *Iris Versicolor* and *Euonymus Atropurpureus*. Both powerfully stimulate the liver, while they do not powerfully stimulate the intestine

of the dog. Although not so powerful as podophyllin, they will both doubtless be preferred in many cases to that substance, because of their far milder excitement of the intestines. For not only is the latter in most cases advantageous on its own account, but also because the action on the liver is far less liable to be hampered and diminished by the intestinal stimulation. This, as we have seen, is apt to be the case with podophyllin. Our experiments on the dog have led us, and have led many others, to try the effect of these substances on man, and they are of great value. The average dose of Iridin is four grains, of Euonymin two grains. In either case two grains of extract of hyoscyamus should be added, and taken at bed time, for without this some persons experience griping. Neither substance produces any sickness or headache. In some persons the above doses of both substances produce a sufficient purgative effect; but in other cases the purgation is insufficient or delayed, and griping is then apt to ensue. The most beneficial result is obtained by following the dose of these remedies by a mild, saline aperient, such as Püllna or Carlsbad Water, on the following morning, so that the bile secreted during the night may be fully and quickly removed. I have in my own case noticed slight depression after four grains of Iridin, which I have never observed after two grains of Euonymin. I therefore inferred that the latter is preferable when repeated stimulation of the liver is desirable. It is, however, important to remember that although Euonymin usually suffices to quickly remove a slight feeling of biliousness, Iridin is, I am convinced, the more powerful remedy of the two, when the tongue is decidedly yellow. I have been in such a case, more than once surprised to find that on awaking in the morning after taking four grains of Iridin the previous night the yellow tongue and bilious sensations were entirely gone. Since the publication of our results these remedies have come into very general use. Mr. Hardyman of Cardiff, (*The British Medical Journal*, July, 12, 1879,) states that he has used Euonymin in two grain doses at bed-time in over fifty cases of biliary derangement and sick headache, and finds it of much value. Finding that in most cases one dose is sufficient, he gives two grains at bed-time on two successive nights, following it each morning with a saline purge."

Composition: The active constituent is an oleo-resin. Whether it contains a distinct principle or alkaloid, is not known, but it is highly probable that such is the case. The important constituent is the oleo-resin, and on the presence of this depends its powers as a hepatic stimulant. It may be administered in the form of tincture, or fluid extract,

or solid extract. The so-called *Iridin* is the oleo-resin, precipitated from a saturated tincture by the addition of water, and mixed with some indifferent powder.

Notwithstanding there is but little tendency to griping manifest in its action, it may be desirable to indicate some method of obviating this. Rutherford suggests the addition of the extract of hyoscyamus—two grains to each dose. One-fourth to one-half grain of extract of belladonna may also be used. A little capsicum seems to be effective. A small quantity of oil of anise, will no doubt accomplish the same object. As, however, delayed action seems to be a cause of the griping, a more active preparation will render any addition to prevent this effect unnecessary. Much of the so-called “*Iridin*” found in commerce but inadequately represents the real powers and capabilities of the remedy.

Bartholow says:—

“It is consequently extremely desirable to have a suitable preparation made which shall contain all of the constituents of the drug. A properly prepared fluid extract, made from the bark of the fresh root, is the only preparation which can adequately represent either *Euonymus* or *Iris*. Such a fluid extract will, under all circumstances, accomplish the results expected from these remedies, whilst the imperfectly prepared *Iridin* or *Euonymin*, will often disappoint. Valuable remedies constantly fall into disfavor, because the preparations do not contain all the principles to be found in them, or in consequence of faulty methods of manufacture, prove to be inert. This statement is eminently true of *Iridin* and *Euonymin*. These resinoids represent these plants in part, only, and hence there cannot be obtained from them the therapeutical results produced by the fluid extracts, which represent these plants in their entirety.”

